

**6.07 MODAFINIL,
Tablet, 100 mg,
ARMODAFINIL
Tablet 50 mg, 150 mg and 250 mg,
Various Sponsors**

1 Purpose of Application

- 1.1 The minor submission from the Australasian Sleep Association (ASA) sought to:
- amend the restriction for modafinil and armodafinil to reflect contemporary guidelines on narcolepsy management;
 - remove the requirement to resubmit sleep study reports before a switch from modafinil to armodafinil (or vice versa).

2 Background

Registration status

- 2.1 Modafinil and armodafinil are TGA registered for the following indications:
- The improvement of wakefulness in patients with excessive daytime sleepiness associated with narcolepsy;
 - Treatment of excessive sleepiness associated with moderate to severe chronic shift work sleep disorder;
 - Adjunct to continuous positive airways pressure (CPAP) in obstructive sleep apnoea/hypopnoea syndrome in order to improve wakefulness.

Previous PBAC consideration

- 2.2 The PBAC previously considered a submission from the ASA requesting an amendment to the PBS listing of modafinil to allow use as first line therapy for the treatment of narcolepsy at its November 2008 meeting.
- 2.3 The key matters of concern from the November 2008 submission are summarised in Table 1.

Public Summary Document – July 2020 PBAC Meeting

Table 1: PBAC matters of concern in previous consideration (November 2008)

Matter of concern	How the resubmission addresses it
The PBAC considered there was insufficient evidence to support the claim that placebo rather than dexamfetamine was the appropriate comparator for modafinil in the first line setting. The Committee noted that the absence of a systematic review of the evidence was a significant impediment to its deliberations. (section 12)	The submission maintained that placebo was the appropriate comparator and provided data from several published meta-analyses comparing modafinil to placebo.
The PBAC did not accept the premise of the submission that from a medical and legal view, dexamfetamine could no longer be considered the standard of care for treatment of narcolepsy. (section 12)	The submission maintained that dexamfetamine could no longer be considered the standard of care for treatment of narcolepsy from a medical and legal view.
The PBAC considered that the omission of an economic analyses was inappropriate. It was noted that modafinil and dexamfetamine had drug costs of \$3327 vs. \$318 per year, respectively, for life long therapy and uncertain relative net clinical effect, particularly in the long term. (section 12)	The resubmission did not present an economic analysis.

Source: Compiled during the evaluation. Section references refer to the November 2008 modafinil PBAC Public Summary Document

2.4 The PBAC has not previously considered armodafinil for first line therapy for the treatment of narcolepsy.

For more detail on PBAC's view, see section 6 PBAC outcome

3 Requested listing

3.1 The submission requested removal of the clinical criteria 'the treatment must be for use when therapy with dexamfetamine poses an unacceptable medical risk; or the treatment must be for use when intolerance to dexamfetamine is of a severity to necessitate treatment withdrawal' from the restriction.

3.2 The submission also requested removing the requirement to resubmit sleep study reports before a switch from modafinil to armodafinil (or vice versa).

3.3 Secretariat suggested additions are in italics and deletions are in strikethrough.

Name, Restriction, Manner of administration and form	PBS item code	Max. qty packs	Max. qty units	№.of Rpts	Proprietary Name and Manufacturer
MODAFINIL modafinil 100 mg tablet, 60	8816B	2	120	5	Various brands and sponsors

Restriction Summary 8665 / Treatment of Concept: 8694

Category / Program: GENERAL – General Schedule (Code GE)
Prescriber type: <input checked="" type="checkbox"/> Medical Practitioners
Restriction type / Method: <input checked="" type="checkbox"/> Authority Required – delayed assessment (In Writing lodged via post or electronic upload)
Indication: Narcolepsy
Treatment Phase: Initial treatment
Administrative Advice: This drug is not PBS-subsidised when used in combination with PBS-subsidised dexamfetamine sulfate or armodafinil.
Treatment criteria: Must be treated by a qualified sleep medicine practitioner or neurologist
Clinical criteria: The treatment must be for use when therapy with dexamfetamine sulfate poses an unacceptable medical risk

Public Summary Document – July 2020 PBAC Meeting

OR
The treatment must be for use when intolerance to dexamfetamine sulfate is of a severity to necessitate treatment withdrawal
AND
Clinical criteria:
Patient must have experienced excessive daytime sleepiness, recurrent naps or lapses into sleep occurring almost daily for at least 3 months
AND
Clinical criteria:
Patient must have a definite history of cataplexy;
OR
Patient must have a mean sleep latency less than or equal to 10 minutes on a Multiple Sleep Latency Test (MSLT);
OR
Patient must have an electroencephalographic (EEG) recording showing the pathologically rapid development of REM sleep
AND
Clinical criteria:
Patient must not have any medical or psychiatric disorder that could otherwise account for the hypersomnia
Prescribing Instructions:
The presence of any one of the following indicates treatment with dexamfetamine sulfate poses an unacceptable medical risk: (a) a psychiatric disorder; (b) a cardiovascular disorder; (c) a history of substance abuse; (d) glaucoma; (e) any other absolute contraindication to dexamfetamine sulfate as specified in the TGA-approved Product Information.
Prescribing Instructions:
The MSLT must be preceded by nocturnal polysomnography. Sleep prior to the MSLT must be at least 6 hours in duration.
Prescribing Instructions:
The authority application must be made in writing and must include the following: (a) a completed authority prescription form; and (b) a completed Narcolepsy Initial PBS authority application and Supporting information form; and (c) details of the contraindication or intolerance to dexamfetamine sulfate; and (d) either: (i) the result and date of the polysomnography test and Multiple Sleep Latency Test (MSLT) conducted by, or under the supervision of, a qualified sleep medicine practitioner; or (ii) the result and date of the electroencephalograph (EEG), conducted by, or under the supervision of, a neurologist. The polysomnography, MSLT or EEG test reports must be provided with the authority application <i>except for the diagnosis of narcolepsy with history of cataplexy.</i>
Administrative Advice:
Any queries concerning the arrangements to prescribe may be directed to Services Australia on 1800 700 270 (hours of operation 8 a.m. to 5 p.m. EST Monday to Friday). Prescribing information (including Authority Application forms and other relevant documentation as applicable) is available on the Services Australia website at www.servicesaustralia.gov.au Applications for authority to prescribe should be submitted online using the form upload facility in Health Professional Online Services (HPOS) at www.servicesaustralia.gov.au/hpos Or mailed to: Services Australia Complex Drugs Reply Paid 9826 HOBART TAS 7004
Administrative Advice:
Any queries concerning the arrangements to prescribe may be directed to Services Australia on 1800 700 270 (hours of operation 8 a.m. to 5 p.m. EST Monday to Friday). Prescribing information (including Authority Application forms and other relevant documentation as applicable) is available on the Services Australia website at www.servicesaustralia.gov.au Applications for authority to prescribe should be submitted online using the form upload facility in Health Professional Online Services (HPOS) at www.servicesaustralia.gov.au/hpos Or mailed to: Services Australia

Public Summary Document – July 2020 PBAC Meeting

Complex Drugs
Reply Paid 9826
HOBART TAS 7001

Name, Restriction, Manner of administration and form	PBS item code	Max. qty packs	Max. qty units	No. of Rpts	Proprietary Name and Manufacturer
ARMODAFINIL					
armodafinil 50 mg tablet, 30	10922W	2	60	5	Nuvigil Teva Pharma Australia Pty Limited
armodafinil 150 mg tablet, 30	10912H	1	30	5	
armodafinil 250 mg tablet, 30	10919Q	1	30	5	

Restriction Summary 8665 / Treatment of Concept: 8694

Category / Program: GENERAL – General Schedule (Code GE)

Prescriber type: Medical Practitioners

Restriction type / Method:

Authority Required – delayed assessment (In Writing lodged via post or electronic upload)

Indication: Narcolepsy

Treatment Phase: Initial treatment

Administrative Advice:

This drug is not PBS-subsidised when used in combination with PBS-subsidised dexamfetamine sulfate or modafinil.

Treatment criteria:

Must be treated by a qualified sleep medicine practitioner or neurologist

Clinical criteria:

~~The treatment must be for use when therapy with dexamfetamine sulfate poses an unacceptable medical risk~~

OR

~~The treatment must be for use when intolerance to dexamfetamine sulfate is of a severity to necessitate treatment withdrawal~~

AND

Clinical criteria:

Patient must have experienced excessive daytime sleepiness, recurrent naps or lapses into sleep occurring almost daily for at least 3 months

AND

Clinical criteria:

Patient must have a definite history of cataplexy;

OR

Patient must have a mean sleep latency less than or equal to 10 minutes on a Multiple Sleep Latency Test (MSLT);

OR

Patient must have an electroencephalographic (EEG) recording showing the pathologically rapid development of REM sleep

AND

Clinical criteria:

Patient must not have any medical or psychiatric disorder that could otherwise account for the hypersomnia

Prescribing Instructions:

~~The presence of any one of the following indicates treatment with dexamfetamine sulfate poses an unacceptable medical risk:~~

- ~~(a) a psychiatric disorder;~~
- ~~(b) a cardiovascular disorder;~~
- ~~(c) a history of substance abuse;~~
- ~~(d) glaucoma;~~
- ~~(e) any other absolute contraindication to dexamfetamine sulfate as specified in the TGA approved Product Information.~~

Prescribing Instructions:

The MSLT must be preceded by nocturnal polysomnography. Sleep prior to the MSLT must be at least 6 hours in duration.

Prescribing Instructions:

The authority application must be made in writing and must include the following:

- (a) a completed authority prescription form; and
- (b) a completed Narcolepsy Initial PBS authority application and Supporting information form; and
- ~~(c) details of the contraindication or intolerance to dexamfetamine sulfate; and~~
- (d) either:

Public Summary Document – July 2020 PBAC Meeting

(i) the result and date of the polysomnography test and Multiple Sleep Latency Test (MSLT) conducted by, or under the supervision of, a qualified sleep medicine practitioner; or
(ii) the result and date of the electroencephalograph (EEG), conducted by, or under the supervision of, a neurologist.
The polysomnography, MSLT or EEG test reports must be provided with the authority application *except for the diagnosis of narcolepsy with history of cataplexy*.

Administrative Advice:

Any queries concerning the arrangements to prescribe may be directed to Services Australia on 1800 700 270 (hours of operation 8 a.m. to 5 p.m. EST Monday to Friday).

Prescribing information (including Authority Application forms and other relevant documentation as applicable) is available on the Services Australia website at www.servicesaustralia.gov.au

Applications for authority to prescribe should be submitted online using the form upload facility in Health Professional Online Services (HPOS) at www.servicesaustralia.gov.au/hpos

Or mailed to:

Services Australia

Complex Drugs

Reply Paid 9826

HOBART TAS 7004

Administrative Advice:

Any queries concerning the arrangements to prescribe may be directed to Services Australia on 1800 700 270 (hours of operation 8 a.m. to 5 p.m. EST Monday to Friday).

Prescribing information (including Authority Application forms and other relevant documentation as applicable) is available on the Services Australia website at www.servicesaustralia.gov.au

Applications for authority to prescribe should be submitted online using the form upload facility in Health Professional Online Services (HPOS) at www.servicesaustralia.gov.au/hpos

Or mailed to:

Services Australia

Complex Drugs

Reply Paid 9826

HOBART TAS 7001

Name, Restriction, Manner of administration and form	PBS item code	Max. qty packs	Max. qty units	No. of Rpts	Proprietary Name and Manufacturer
MODAFINIL modafinil 100 mg tablet, 60	8816B	2	120	5	Various brands and sponsors
ARMODAFINIL armodafinil 50 mg tablet, 30	10922W	2	60	5	Nuvigil Teva Pharma Australia Pty Limited
armodafinil 150 mg tablet, 30	10912H	1	30	5	
armodafinil 250 mg tablet, 30	10919Q	1	30	5	

Restriction Summary 8664 / Treatment of Concept: 6547 (modafinil and armodafinil)

Category / Program: GENERAL – General Schedule (Code GE)

Prescriber type: Medical Practitioners

Restriction type / Method:

Authority Required – immediate assessment (Telephone/online)

Indication: Narcolepsy

Treatment Phase: continuing treatment or switching between modafinil/armodafinil

Administrative Advice:

This drug is not PBS-subsidised when used in combination with PBS-subsidised dexamfetamine sulfate or armodafinil/modafinil.

Clinical criteria:

Patient must have previously received PBS-subsidised treatment with this drug modafinil/armodafinil for this condition

Administrative Advice:

Authority applications for continuing treatment may be made by telephone to the Department of Human Services on 1800 700 270 (hours of operation 8 a.m. to 5 p.m. EST Monday to Friday).

Administrative Advice:

Any queries concerning the arrangements to prescribe may be directed to Services Australia on 1800 700 270 (hours of operation 8 a.m. to 5 p.m. EST Monday to Friday).

Public Summary Document – July 2020 PBAC Meeting

<p>Prescribing information (including Authority Application forms and other relevant documentation as applicable) is available on the Services Australia website at www.servicesaustralia.gov.au Applications for authority to prescribe should be submitted online using the form upload facility in Health Professional Online Services (HPOS) at www.servicesaustralia.gov.au/hpos Or mailed to: Services Australia Complex Drugs Reply Paid 9826 HOBART TAS 7004</p>
<p>Administrative Advice: Applications for authorisation under this restriction may be made in real time using the Online PBS Authorities system (see www.servicesaustralia.gov.au/HPOS) or by telephone by contacting Services Australia on 1800 700 270 (hours of operation 8 a.m. to 5 p.m. EST Monday to Friday).</p>

- 3.4 The pre-PBAC response noted the suggested amendments to the continuing restriction and considered that the proposed changes would remove unnecessary administrative burden and allow more efficient delivery of care to patients.
- 3.5 The Secretariat/Services Australia requested clarification from the PBAC whether polysomnography, Multiple Sleep Latency Test (MSLT) or electroencephalography (EEG) tests are required for narcolepsy patients with history of cataplexy. Currently the prescriber instructions require all the test reports to be submitted to Services Australia, including in a diagnosis of cataplexy.
- 3.6 The pre-PBAC response advised that both MSLT and polysomnography are part of clinical practice and would be undertaken to confirm the diagnosis of narcolepsy, however isolated EEG testing outside of sleep studies is not routinely performed.

For more detail on PBAC's view, see section 6 PBAC outcome

4 Comparator

- 4.1 The previous submission considered by the PBAC in November 2008 nominated “no treatment” as the main comparator. This was unchanged.
- 4.2 The PBAC previously considered there was insufficient evidence to support the claim that placebo rather than dexamfetamine was the appropriate comparator for modafinil in the first line setting (November 2008 PBAC meeting).
- 4.3 The PBAC could only recommend listing modafinil and armodafinil at a higher price than the alternative therapy if it is satisfied that they provide, for some patients, a significant improvement in efficacy or reduction of toxicity over the alternative therapy or therapies (National Health Act 1953, Section 101(3B)). If the committee is so satisfied, it must make a statement to this effect. The alternative therapies in this case should include dexamfetamine.
- 4.4 The pre-PBAC response suggested that dexamfetamine is artificially entrenched as first line treatment due to PBS restrictions, rather than high-level clinical evidence. Therefore, the ASA maintained that placebo was the most appropriate comparator to the use of modafinil and armodafinil in the first line setting.

For more detail on PBAC's view, see section 6 PBAC outcome

5 Consideration of the evidence

Sponsor hearing

5.1 There was no hearing for this item as it was a minor submission.

Consumer comments

5.2 The PBAC noted that no consumer comments were received for this item.

Clinical evidence

5.3 Details of the studies presented in the submission are provided in the table below.

Table 2: Trials and associated reports presented in the submission

Author/s	Publication title	Publication citation
Golicki, D., et al	Modafinil for narcolepsy: Systematic review and meta-analysis.	<i>Med Sci Mon Int Med J Exp Clin Res</i> 2010; 16(8): p.RA177-186.
Lehert, P. and B. Falissard	Multiple treatment comparison in narcolepsy: A network meta-analysis.	<i>Sleep</i> 2018; 41(12)
Mitler, M.M, et al	Treatment of narcolepsy with methamphetamine	<i>Sleep</i> 1993; 16(4): p. 306-17.
Schindler, J., et al	Amphetamine, mazindol, and fencamfamin in narcolepsy	<i>Br Med J (Clin Res Ed)</i> 1985; 290(6476): p. 1167-70.

5.4 As a minor submission, no evaluation of the referenced studies was undertaken.

5.5 The ASA commented that international guidelines, practical guidance, and consensus publications recommended modafinil and armodafinil to be used as first line therapy and dexamfetamine second/third line therapy for narcolepsy.

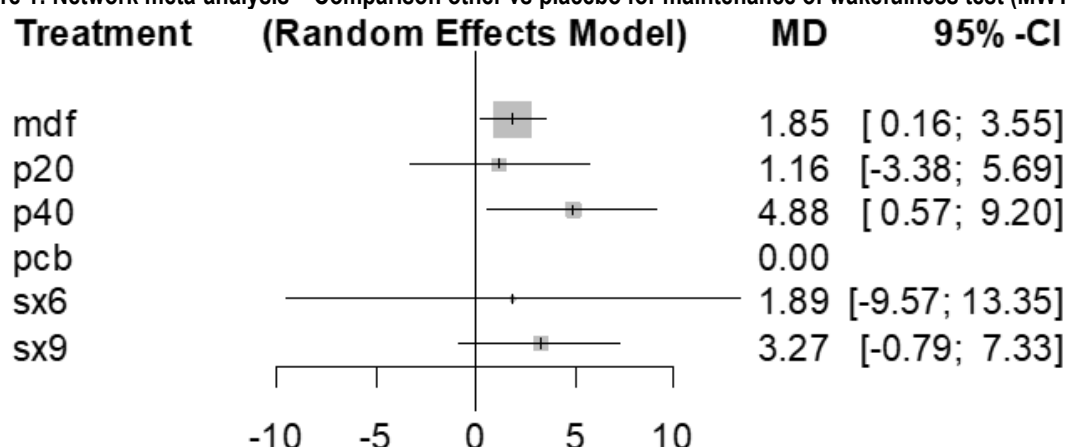
5.6 The submission noted that the Australian Therapeutic Guidelines (TGs) recommend modafinil and armodafinil as a first line treatment for increasing alertness, alongside dexamfetamine and methylphenidate. The TGs note that no studies directly compare modafinil and armodafinil with dexamfetamine and methylphenidate for the treatment for sleepiness, but modafinil and armodafinil have fewer side-effects.¹

Comparative effectiveness

5.7 The results of the meta-analysis for several narcolepsy treatments for the maintenance of wakefulness test (MWT) are presented in Figure 1.

¹ https://tgldcdp.tg.org.au/viewTopic?topicfile=idiopathic-hypersomnolence-and-narcolepsy&guidelineName=Neurology&topicNavigation=navigateTopic#toc_d1e83

Figure 1: Network meta-analysis – Comparison other vs placebo for maintenance of wakefulness test (MWT)



mdf = modafinil; p20 and p40 = pitolisant 20 and 40mg respectively; pcb = placebo; sx6 and sx9 = sodium oxybate 6 and 9mg respectively.

Source: Figure 1, pg. 6 of the submission

5.8 The submission claimed that the results demonstrated that for MWT modafinil was statistically significantly better than placebo.

5.9 The submission reported that in the meta-analysis published by Golicki et al, there was a statistically significant improvement in MWT for modafinil versus placebo, with a mean difference in the parallel studies of 2.81 (2.10, 3.53). The submission argued that the meta-analysis (Golicki et al) also highlighted that modafinil appeared superior in terms of mean sleep latency when compared to placebo (mean difference 1.11 (0.55, 1.66)).

Comparative harms

5.10 The submission presented the risk differences between modafinil and placebo as reported by Golicki et al (Table 3), and the adverse events reported for dexamfetamine from Mitler et al and Schindler et al (Table 4).

Table 3: Adverse events - Risk difference modafinil vs. placebo

	Number of study	Risk difference effect size (95% CI)
Nervousness	3	0.02 (-0.02, 0.06)
Headache	5	0.03 (-0.07, 0.13)
Pain	2	-0.03 (-0.09, 0.02)
Back pain	3	0.01 (-0.07, 0.08)
Flu syndrome	2	0.04 (-0.02, 0.09)
Nausea	4	0.07 (0.03, 0.11)
Diarrhoea	3	0.04 (0.00, 0.07)
Dyspepsia	3	-0.00 (-0.05, 0.04)
Dry mouth	3	0.01 (-0.08, 0.10)
Dizziness	2	-0.04 (-0.13, 0.05)
Rhinitis	2	0.03 (-0.05, 0.12)
Pharyngitis	2	-0.00 (-0.05, 0.04)
Dysmenorrhea	2	-0.01 (-0.07, 0.04)

Source: Table 4, pg. 7 of the submission. Bold: statistically significant

Table 4: Adverse events of dexamfetamine

	Placebo	Methamphetamine/amphetamine/ Dexamfetamine (10-20 mg/day)	Methamphetamine/amphetamine/ Dexamfetamine (30-60 mg/day)
Sweaty	6	5	3
Palpitations	2	1	2
On edge	7	6	4
Nervousness	0	2	2
Insomnia	0	1	5
Headache	1	3	4
Akathisia	0	2	3
Chest discomfort	0	1	1
Abdominal pain	0	1	1
Loss of appetite	0	4	3

Source: submission Table 2

- 5.11 The submission claimed that the results of the Golicki et al. network meta-analysis indicated that modafinil had a balanced profile for efficacy and safety compared to placebo. The submission noted that only nausea and diarrhoea were statistically significantly more frequent with modafinil when compared to placebo (Table 3).
- 5.12 The submission argued that only nervousness and headache were common adverse events (AEs) for patients on modafinil (Table 3), whereas patients on dexamfetamine were 2 to 3 times more likely to have these AEs than patients on placebo (Table 4).
- 5.13 The PBAC has previously considered that armodafinil is non-inferior to modafinil in terms of comparative safety (para 7.2, armodafinil Public Summary Document, March 2016 PBAC meeting). Therefore, the ASA concluded that the safety profile of armodafinil would be similar to that of modafinil in the evidence presented.
- 5.14 The submission noted that dexamfetamine is a Schedule 8 medicine with detrimental short- and long-term effects, including tolerance (necessitating higher doses), risk of addiction and potential harm of cardiac arrhythmias and psychiatric disturbances.
- 5.15 The pre-PBAC response considered that the long-term adverse event profile of dexamfetamine does not support the benefit to risk ratio; noting that 58 adverse drug reaction reports regarding dexamfetamine were made to the TGA in the period 2005 to 2020, including two deaths.

Clinical claim

- 5.16 The submission claimed superior comparative effectiveness and safety of modafinil and armodafinil compared with dexamfetamine.
- 5.17 No clinical evidence comparing modafinil and armodafinil to dexamfetamine was provided to support the clinical claim.
- 5.18 The pre-PBAC response advised that there is little clinical data available to facilitate a comparison of dexamfetamine with armodafinil and modafinil.
- 5.19 The PBAC considered that the claim of superior comparative effectiveness was not adequately supported by the data.

- 5.20 The PBAC considered that the claim of superior comparative safety was not adequately supported by the data.

Economic analysis

- 5.21 The resubmission did not present an economic analysis.
- 5.22 The PBAC previously considered that the omission of an economic analysis was inappropriate (section 12, modafinil Public Summary Document (PSD), November 2008 PBAC Meeting).

Drug cost/patient/year

Modafinil \$2,425

- 5.23 The estimated drug cost/patient per year was \$2,425, based on a daily dose of 400 mg (i.e. 12 prescriptions per year at a DPMQ of \$202.11).

Armodafinil \$3,007

- 5.24 The estimated drug cost/patient per year was \$3,007, based on a daily dose of 250 mg (i.e. 12 prescriptions per year at a DPMQ \$250.56).

Estimated PBS usage & financial implications

- 5.25 No financial estimates were provided in the submission.
- 5.26 The June 2019 Drug Utilisation Sub-Committee (DUSC) analysis showed:
- the number of patients on therapy for narcolepsy had increased following the PBS listing of armodafinil;
 - dexamfetamine was the most used drug for narcolepsy by prescription volume and number of prevalent patients from 2015-2018, inclusive;
 - there was a steep increase in the number of patients starting dexamfetamine for narcolepsy from 178 patients in the second quarter of 2018 to 465 patients in the fourth quarter of 2018, which coincided with a 35.9% increase in patients new to narcolepsy therapy from 2017 to 2018.

For more detail on PBAC's view, see section 6 PBAC outcome

6 PBAC Outcome

- 6.1 The PBAC deferred making a recommendation to change the listing of modafinil and armodafinil on the PBS to allow use as first line therapy for the treatment of narcolepsy to request the Department undertake further analysis of what data are available to assess comparative cost-effectiveness and determine the financial implications of the proposed change.
- 6.2 The PBAC recommended minor adjustments to the existing listings to clarify that resubmitting sleep study reports during a switch from modafinil to armodafinil (or vice versa) need not occur.

Public Summary Document – July 2020 PBAC Meeting

- 6.3 The PBAC considered that it was unnecessary to provide MSLT + polysomnography results or EEG recording to Services Australia for patients with a definite history of cataplexy. Given this, delayed assessment of a written Authority Required application in these cases is not required. A separate initial listing (telephone/online) for patients with a definite history of cataplexy would facilitate this, with authority for patients without cataplexy remaining as written and retaining requirement for MSLT and EEG. The Secretariat advised marking this new listing as a 'Complex Authority Required (CAR)' for consistency with the existing listing.
- 6.4 The PBAC recalled that it was the large difference between the prices of modafinil and dexamfetamine which justified a second-line indication and a comparison with placebo (section 12, modafinil PSD, November 2008 PBAC meeting). The PBAC considered that the most appropriate comparator for modafinil and armodafinil in the first line setting was dexamfetamine.
- 6.5 The PBAC considered that the ASA had raised an important question around the relative safety of dexamfetamine compared to modafinil/armodafinil but that the evidence presented was insufficient.
- 6.6 The PBAC noted that, under section 101(3B) of the Act, a significant improvement in efficacy or reduction of toxicity over the alternative therapy or therapies is required to list modafinil and armodafinil at a higher price than dexamfetamine at the same place in therapy. The PBAC noted no clinical evidence directly comparing modafinil and armodafinil to dexamfetamine was provided to support the clinical claim of superior comparative effectiveness and safety and therefore concluded there was insufficient evidence to support a higher price.
- 6.7 The Committee considered that due to the significant cost difference between modafinil/armodafinil and dexamfetamine (\$2,425/\$3,007 vs. \$279 per patient/year respectively), permitting use of modafinil/armodafinil in the first line setting would have significant financial implications.
- 6.8 The PBAC requested the Department seek further information on the financial implications of a first line listing of modafinil/armodafinil for the treatment of narcolepsy.
- 6.9 The PBAC noted in the DUSC report that a substantial number of patients initiated treatment for narcolepsy with modafinil or armodafinil. The PBAC was uncertain whether the difference in the treatment algorithm between the PBS restriction (dexamfetamine as first line) and clinical guidelines (modafinil/armodafinil as first line) may be contributing to this.
- 6.10 The PBAC considered in practice both polysomnography and MSLT testing would be undertaken to confirm diagnosis of narcolepsy patients with history of cataplexy. However, the PBAC advised the clinical criteria of the PBS restriction for modafinil/armodafinil does not require polysomnography, MSLT or EEG tests for these patients and recommended amending the restriction criteria to reflect this.

Public Summary Document – July 2020 PBAC Meeting

Outcome:

Deferred

7 Recommended listing

7.1 Amend the existing Initial treatment listings for modafinil (8816B) and armodafinil (10912H, 10919Q and 10922W) as follows:

Name, Restriction, Manner of administration and form	PBS item code	Max. qty packs	Max. qty units	No. of Rpts	Proprietary Name and Manufacturer
MODAFINIL modafinil 100 mg tablet, 60	8816B	2	120	5	Various brands and sponsors

Name, Restriction, Manner of administration and form	PBS item code	Max. qty packs	Max. qty units	No. of Rpts	Proprietary Name and Manufacturer
ARMODAFINIL armodafinil 50 mg tablet, 30	10922W	2	60	5	Nuvigil Teva Pharma Australia Pty Limited
armodafinil 150 mg tablet, 30	10912H	1	30	5	
armodafinil 250 mg tablet, 30	10919Q	1	30	5	

Restriction Summary 8665 / Treatment of Concept: 8694

Category / Program: GENERAL – General Schedule (Code GE)
Prescriber type: <input checked="" type="checkbox"/> Medical Practitioners
Restriction type / Method: <input checked="" type="checkbox"/> Authority Required – delayed assessment (Written application lodged via post or electronic upload)
Indication: Narcolepsy
Treatment Phase: Initial treatment of narcolepsy without cataplexy
Administrative Advice: [currently MODAFINIL SPECIFIC – make generic] This drug is not PBS-subsidised when used in combination with PBS-subsidised dexamfetamine sulfate or armodafinil/modafinil.
Administrative Advice: [currently ARMODAFINIL SPECIFIC – make generic] This drug is not PBS-subsidised when used in combination with PBS-subsidised dexamfetamine sulfate or armodafinil/modafinil.
Treatment criteria:
Must be treated by a qualified sleep medicine practitioner or neurologist
Clinical criteria:
The treatment must be for use when therapy with dexamfetamine sulfate poses an unacceptable medical risk; or
The treatment must be for use when intolerance to dexamfetamine sulfate is of a severity to necessitate treatment withdrawal
AND
Clinical criteria:
Patient must have experienced excessive daytime sleepiness, recurrent naps or lapses into sleep occurring almost daily for at least 3 months
AND
Clinical criteria:
Patient must have a definite history of cataplexy; or
Patient must have a mean sleep latency less than or equal to 10 minutes on a Multiple Sleep Latency Test (MSLT); or
Patient must have an electroencephalographic (EEG) recording showing the pathologically rapid development of REM sleep
AND
Clinical criteria:

Public Summary Document – July 2020 PBAC Meeting

Patient must not have any medical or psychiatric disorder that could otherwise account for the hypersomnia
<p>Prescribing Instructions: The presence of any one of the following indicates treatment with dexamfetamine sulfate poses an unacceptable medical risk:</p> <p>(a) a psychiatric disorder; (b) a cardiovascular disorder; (c) a history of substance abuse; (d) glaucoma; (e) any other absolute contraindication to dexamfetamine sulfate as specified in the TGA-approved Product Information.</p>
<p>Prescribing Instructions: The MSLT must be preceded by nocturnal polysomnography. Sleep prior to the MSLT must be at least 6 hours in duration.</p>
<p>Prescribing Instructions: The authority application must be made in writing and must include the following:</p> <p>(a) a completed authority prescription form; and (b) a completed Narcolepsy Initial PBS authority application and Supporting information form; and (c) details of the contraindication or intolerance to dexamfetamine sulfate; and (d) either: (i) the result and date of the polysomnography test and Multiple Sleep Latency Test (MSLT) conducted by, or under the supervision of, a qualified sleep medicine practitioner; or (ii) the result and date of the electroencephalograph (EEG), conducted by, or under the supervision of, a neurologist. The polysomnography, MSLT or EEG test reports must be provided with the authority application <i>except for the diagnosis of narcolepsy with history of cataplexy.</i></p>
<p>Administrative Advice: Any queries concerning the arrangements to prescribe may be directed to Services Australia on 1800 700 270 (hours of operation 8 a.m. to 5 p.m. EST Monday to Friday).</p> <p>Prescribing information (including Authority Application forms and other relevant documentation as applicable) is available on the Services Australia website at www.servicesaustralia.gov.au</p> <p>Applications for authority to prescribe should be submitted online using the form upload facility in Health Professional Online Services (HPOS) at www.servicesaustralia.gov.au/hpos</p> <p>Or mailed to: Services Australia Complex Drugs Reply Paid 9826 HOBART TAS 7001</p>

7.2 Create 2 new Initial treatment listings (1 new listing for modafinil and 1 new listing for armodafinil) for narcolepsy with cataplexy as follows:

Name, Restriction, Manner of administration and form	PBS item code	Max. qty packs	Max. qty units	No. of Rpts	Proprietary Name and Manufacturer
MODAFINIL modafinil 100 mg tablet, 60	8816B	2	120	5	Various brands and sponsors

Name, Restriction, Manner of administration and form	PBS item code	Max. qty packs	Max. qty units	No. of Rpts	Proprietary Name and Manufacturer
ARMODAFINIL armodafinil 50 mg tablet, 30	10922W	2	60	5	Nuvigil Teva Pharma Australia Pty Limited
armodafinil 150 mg tablet, 30	10912H	1	30	5	
armodafinil 250 mg tablet, 30	10919Q	1	30	5	

Public Summary Document – July 2020 PBAC Meeting

Create 2 new Restriction Summaries [NEW] Treatment of Concept: [NEW] (1 for modafinil, 1 for armodafinil)

Category / Program: GENERAL – General Schedule (Code GE)
Prescriber type: <input checked="" type="checkbox"/> Medical Practitioners
Restriction type / Method: <input checked="" type="checkbox"/> Authority Required – immediate assessment (Telephone/Online)
Indication: Narcolepsy
Treatment Phase: Initial treatment of narcolepsy with cataplexy
Administrative Advice: [currently MODAFINIL SPECIFIC – make generic] This drug is not PBS-subsidised when used in combination with PBS-subsidised dexamfetamine sulfate or armodafinil/modafinil.
Administrative Advice: [currently ARMODAFINIL SPECIFIC – make generic] This drug is not PBS-subsidised when used in combination with PBS-subsidised dexamfetamine sulfate or armodafinil/modafinil.
Treatment criteria: Must be treated by a qualified sleep medicine practitioner or neurologist
Clinical criteria: The treatment must be for use when therapy with dexamfetamine sulfate poses an unacceptable medical risk; or The treatment must be for use when intolerance to dexamfetamine sulfate is of a severity to necessitate treatment withdrawal
AND
Clinical criteria: Patient must have experienced excessive daytime sleepiness, recurrent naps or lapses into sleep occurring almost daily for at least 3 months
AND
Clinical criteria: Patient must have a definite history of cataplexy documented in their medical records for auditing purposes; or
AND
Clinical criteria: Patient must not have any medical or psychiatric disorder that could otherwise account for the hypersomnia
Prescribing Instructions: The presence of any one of the following indicates treatment with dexamfetamine sulfate poses an unacceptable medical risk: (a) a psychiatric disorder; (b) a cardiovascular disorder; (c) a history of substance abuse; (d) glaucoma; (e) any other absolute contraindication to dexamfetamine sulfate as specified in the TGA-approved Product Information.
Administrative Advice: Applications for authorisation under this restriction may be made in real time using the Online PBS Authorities system (see www.servicesaustralia.gov.au/HPOS) or by telephone by contacting Services Australia on 1800 700 270 (hours of operation 8 a.m. to 5 p.m. EST Monday to Friday).

7.3 Amend the existing Continuing treatment listings for modafinil (8816B) and armodafinil (10912H, 10919Q and 10922W) as follows:

Name, Restriction, Manner of administration and form	PBS item code	Max. qty packs	Max. qty units	No. of Rpts	Proprietary Name and Manufacturer
MODAFINIL modafinil 100 mg tablet, 60	8816B	2	120	5	Various brands and sponsors
ARMODAFINIL armodafinil 50 mg tablet, 30	10922W	2	60	5	Nuvigil Teva Pharma Australia Pty Limited
armodafinil 150 mg tablet, 30	10912H	1	30	5	
armodafinil 250 mg tablet, 30	10919Q	1	30	5	

Restriction Summary 8664 / Treatment of Concept: 6547 (modafinil and armodafinil)

Category / Program: GENERAL – General Schedule (Code GE)

Public Summary Document – July 2020 PBAC Meeting

Prescriber type: <input checked="" type="checkbox"/> Medical Practitioners
Restriction type / Method: <input checked="" type="checkbox"/> Authority Required – immediate assessment (Telephone/Online)
Indication: Narcolepsy
Treatment Phase: Continuing treatment or switching between modafinil/armodafinil
Administrative Advice: This drug is not PBS-subsidised when used in combination with PBS-subsidised dexamfetamine sulfate or armodafinil/modafinil.
Clinical criteria: Patient must have previously received PBS-subsidised treatment with this drug modafinil/armodafinil for this condition
Administrative Advice: Authority applications for continuing treatment may be made by telephone to the Department of Human Services on 1800 700 270 (hours of operation 8 a.m. to 5 p.m. EST Monday to Friday).
Administrative Advice: Applications for authorisation under this restriction may be made in real time using the Online PBS Authorities system (see www.servicesaustralia.gov.au/HPOS) or by telephone by contacting Services Australia on 1800 700 270 (hours of operation 8 a.m. to 5 p.m. EST Monday to Friday).
Administrative Advice: Any queries concerning the arrangements to prescribe may be directed to Services Australia on 1800 700 270 (hours of operation 8 a.m. to 5 p.m. EST Monday to Friday). Prescribing information (including Authority Application forms and other relevant documentation as applicable) is available on the Services Australia website at www.servicesaustralia.gov.au Applications for authority to prescribe should be submitted online using the form upload facility in Health Professional Online Services (HPOS) at www.servicesaustralia.gov.au/hpos Or mailed to: Services Australia Complex Drugs Reply Paid 9826 HOBART TAS 7001
Administrative Advice: If this application is for a treatment switch between PBS-subsidised modafinil and armodafinil, previously submitted test results for polysomnography/MSLT/EEG need not be resubmitted.

The restrictions may be subject to further review. Should there be any changes made to the restrictions the Sponsors will be informed.

8 Context for Decision

The PBAC helps decide whether and, if so, how medicines should be subsidised through the Pharmaceutical Benefits Scheme (PBS) in Australia. It considers applications regarding the listing of medicines on the PBS and provides advice about other matters relating to the operation of the PBS in this context. A PBAC decision in relation to PBS listings does not necessarily represent a final PBAC view about the merits of the medicine or the circumstances in which it should be made available through the PBS. The PBAC welcomes applications containing new information at any time.

9 Sponsor's Comment

The sponsor had no comment.